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2. Patent application number *(The Patent Office will fill in this part)* 0319817.3

22 AUG 2003

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

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Patents ADP number *(if you know it)* 56608730065

If the applicant is a corporate body, give the country/state of its incorporation Denmark

4. Title of the invention Microcapsules, method for preparing same and use thereof

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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Stephen J. Avery
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Microcapsules, method for preparing same and use thereof

Field of the invention

The present invention relates to microcapsules, and more particularly to microcapsules where an encapsulated aqueous bead or encapsulated aqueous beads comprising the active ingredient or active ingredients is/are further encapsulated in a hydrophobic shell matrix. The present invention relates also to novel methods for preparing the microcapsules according to the invention, as well as to the use of the microcapsules of the present invention.

Background of the invention

US patent 5,204,029 discloses a process for preparing edible microcapsules which contain a multiplicity of liquid cores. In the process, a water-in-oil emulsion, with the active ingredient dissolved in an inner aqueous phase, is spray cooled, which causes the solidification of the fat phase and the entrapment of the aqueous phase as minute droplets dispersed in a microcapsule. This process, however, leads to very unstable microcapsules from which the water phase migrates from the inner part of the microcapsule to an outer part. This further results in the condensation of the water on the wall of a container.

Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. Vol. 15, pp. 473 to 474, discloses a process in which liquids are encapsulated using a rotating extrusion head containing concentric nozzles. The process is only suitable for liquids or slurries, and the products of the process are large beads having meltable coatings, such as fats or waxes. However, the microcapsules containing a single liquid droplet as a core are very susceptible to rupture.

In their article "Mass preparation and characterization of alginate microspheres" in Process Biochemistry 35 (2000) 885 to 888 Mofidi, N. et al. describe a method for mass preparation of microspheres, in which method a sterilized alginate solution is prepared and the solution is then poured into a reactor containing a non-aqueous phase, while being stirred. An emulsion of alginate microdroplets is formed and an appropriate amount of the cross-linker is added. Microspheric alginate-gel particles fell to the bottom and they were collected by filtration.

Similarly, Wong, T.W. et al in J. Microencapsulation, 2002 Vol. 19, no 4, 511 to 522, describe release characteristics from pectin microsphperes and the method for preparing these microspheres. In this method, pectin mi-

crospheres are prepared by a water-in-oil emulsion technique, in which minute droplets of pectin containing an active ingredient dispersed in a liquid hydrophobic continuous phase are hardened and collected by filtration.

Microencapsulation by a coacervation-phase separation process is known from an article by Joseph A. Bakan in Controlled Release Technologies, 1980 by Agis F. Kydonieus. The process consists of a series of three steps carried out under continuous agitation: (1) formation of three immiscible chemical phases; (2) deposition of the coating; and (3) rigidization of the coating.

Sanghvi, S.P. and Naim J.G. have studied the effect of viscosity and interfacial tension on the particle size of cellulose acetate trimellitate microspheres. The results are presented in their article in J. Microencapsulation, 1992, Vol. 9, no 2, 215 to 227.

In their article in Lebensm. -Wiss. u. -Technol., 33, 80 to 88 (2000) Lee, S.J. and Rosenberg, M. describe a double emulsification and heat gelation process for preparing whey protein-based microcapsules. The microcapsules prepared according to the described process are whey protein-based microcapsules containing an apolar core material.

In their article in Science Vol. 298, 1 November 2002, Dinsmore et al. describe selectively permeable capsules composed of colloidal particles. The capsules are fabricated by the self-assembly of colloidal particles onto the interface of emulsion droplets. After the particles are locked together to form elastic shells, the emulsion droplets are transferred to a fresh continuous-phase fluid that is the same as that inside the droplets.

A disadvantage of the microcapsules or spheres prepared according to the cited references of Lee et al, Dinsmore et al, Mofidi et al or Wong et al is that the microcapsules are only single encapsulated microcapsules and the hydrophobic phase is discarded after the microcapsules have been prepared.

A problem associated with the prior art microcapsules containing only one single liquid phase droplet is that they are very susceptible to rupture. The shell material can break for example during storing or handling of the microcapsules, and this causes the liquid of the whole inner phase to run free. This results in a sticky mass, and the microcapsules are no longer in the form of a free flowing powder.

This problem of rupturing can be somewhat alleviated by preparing microcapsules which contain a multiplicity of liquid cores, as described in the

US patent 5,204,029. However, this process still results in very unstable microcapsules from which the water phase migrates from the inner part of the microcapsule to the outer part and further outside the capsule. This further results in the condensation of water on the wall of the container. Another problem associated with the microcapsules according to the cited US patent 5,204,029 is that the release of the active ingredient cannot be controlled in the microcapsules.

The present invention seeks to overcome the problems of the known microcapsules, as described above, by providing microcapsules which are very stable and which provide a controlled and/or sustained release of the active ingredient.

Brief description of the invention

An object of the present invention is thus to provide microcapsules comprising a solidified hydrophobic shell matrix, encapsulated aqueous bead or beads which is/are further encapsulated in the solidified hydrophobic shell matrix, and an active ingredient or active ingredients dissolved or incorporated in the encapsulated aqueous bead or beads, and methods for the preparation thereof, so as to solve the above mentioned problems. The objects of the invention are achieved by microcapsules and a method for preparing microcapsules, which are characterized by what is stated in the independent claims. Preferred embodiments of the invention are disclosed in the dependent claims.

Accordingly, as one aspect, the present invention provides a microcapsule which comprises a solidified hydrophobic shell matrix, an encapsulated aqueous bead or beads encapsulated in the solidified hydrophobic shell matrix, and an active ingredient or active ingredients dissolved or incorporated in the encapsulated aqueous bead or beads.

As another aspect, the invention provides a method for preparing microcapsules, which method comprises the steps of

a) providing an aqueous phase and an active ingredient or active ingredients dissolved or incorporated in the aqueous phase,

b) providing a hydrophobic phase in melted form,

c) incorporating or dissolving an encapsulating material or mixture of encapsulating materials in the aqueous phase or in the hydrophobic phase,

d) combining the aqueous phase with the hydrophobic phase and homogenizing or mixing the combined phases to form a water-in-oil emulsion,

e) encapsulating the aqueous phase in the emulsion, thus convert-

ing the liquid aqueous phase into encapsulated aqueous beads, whereby a dispersion comprising aqueous beads is formed and the active ingredient or active ingredients are dissolved or incorporated in the aqueous beads, and

f) processing the dispersion obtained in step e) to form microcapsules where the encapsulated aqueous beads are further encapsulated in the solidified hydrophobic shell matrix.

A further aspect of the present invention relates to the use of the microcapsules of the present invention in food/feed industry and in pharmaceutical or cosmetic applications.

The invention is based on the concept of adding an encapsulating material, for example a hydrocolloid or any other suitable encapsulating material or mixture thereof, to the aqueous phase comprising the active ingredient(s) or to the hydrophobic phase in melted form, forming an emulsion of the aqueous phase and of the melted hydrophobic phase and, subsequently, encapsulating the active ingredient(s) in an aqueous bead or beads in the emulsion. The encapsulation of the aqueous phase is performed by gelling, cross-linking, coacervation, sintering or by any other suitable means. This results in dispersion where encapsulated aqueous beads comprising the active ingredient are dispersed in the hydrophobic phase. The dispersion is cooled below the melting or dropping point of the hydrophobic phase by any suitable process, which results in the formation of microcapsules. The cooling process can be performed, for example by spray cooling or fluidized bed cooling. The microcapsules comprise a number of encapsulated aqueous beads, which further contain the active ingredient(s), and the encapsulated aqueous beads are further encapsulated in a solidified hydrophobic shell matrix.

An advantage of the present invention is that the release of the active ingredient(s) from the microcapsules can be controlled. The release rate of a water-soluble active ingredient in a conventionally spray cooled fat matrix microcapsule is usually not controlled by the melting of the fat matrix but rather by the diffusion of water into the microcapsule and subsequent migration of the active ingredient outside the microcapsule. The release rate of the active ingredient from conventional spray cooled microcapsules is usually very high. Typically, the release rates of the active ingredients are in the range of approximately 80% release within 15 minutes, depending on the nature of the encapsulated active ingredient. The novel and inventive microcapsules of the present invention have a much lower rate and/or sustained release of the ac-

tive ingredients since most of the active ingredients are released when the solidified hydrophobic shell matrix is actually "melted". The release of the active ingredients from the microcapsules of the present invention can be controlled and the release can be initiated in various ways, for example by heat treatment, e.g. by heating, such as in a microwave oven, or by freezing, by stress treatment or by any other suitable process. The release of the active ingredients from the microcapsules of the present invention can also be sustained or it can happen very slowly.

Another advantage of the microcapsules of the present invention is that the stability of the microcapsules is improved. Since the active ingredients are dissolved or incorporated in encapsulated, preferably in gelled or cross-linked aqueous beads, which are further encapsulated in the solidified hydrophobic shell matrix, the aqueous phase is not able to migrate or evaporate to the shell matrix or outside the shell matrix.

An advantage of the microcapsules of the present invention compared to the microcapsules of the prior art, for example microcapsules prepared according to the cited references of Lee et al, Dinsmore et al, Mofidi et al or Wong et al, is that the hydrophobic phase is used to form a further encapsulation, thus forming microcapsules, where the active ingredient(s) is/are first encapsulated inside an aqueous bead and then further encapsulated in a hydrophobic phase.

The new improved properties of the microcapsules of the present invention enable the use of the microcapsules of the present invention in a wide variety of applications, for example in various applications in the food /feed or pharmaceutical fields.

Yet another advantage of the method of the invention is that it enables a high production capacity to be achieved while the costs are still low.

Brief description of the drawings

In the following, the invention will be described in greater detail by means of preferred embodiments and with reference to the examples.

Figure 1 is a graphical presentation of the results of Example 7. It illustrates the comparison between release rates of encapsulated and conventionally spray cooled calcium propionate.

Detailed description of the invention

The present invention relates to microcapsules which comprise a

solidified hydrophobic shell matrix, an encapsulated aqueous bead or beads which is/are further encapsulated in the solidified hydrophobic shell matrix, and an active ingredient or active ingredients dissolved or incorporated in the encapsulated aqueous bead or beads.

Preferably, the aqueous bead contains an encapsulating material, such as a hydrocolloid or any other suitable encapsulating material or mixture thereof in a concentration suitable to be susceptible to gelling, cross-linking, coacervation or sintering. Preferably, the encapsulated aqueous bead is a gelled or cross-linked hydrocolloid bead.

According to one aspect of the present invention, the active ingredient or active ingredients is/are double encapsulated in the microcapsules. First, the active ingredient is dissolved or incorporated in an aqueous phase containing encapsulating material, such as hydrocolloid or any other suitable encapsulating material or mixture thereof, and the aqueous phase is encapsulated, for example by gelling, cross-linking, coacervation, sintering or by any other suitable means, and the resulting encapsulated aqueous bead or beads is/are further encapsulated in a solidified hydrophobic shell matrix.

The hydrophobic shell matrix is selected based on desired properties of the microcapsule, for example based on the intended use of the microcapsules, storage temperature, etc. The hydrophobic shell matrix should have a melting point above 45°C so that it can be stored at room temperature, in general any hydrophobic material can be used if the microcapsules are stored below the melting temperature of the hydrophobic material.

In this application, melted form means that the hydrophobic phase is at the lowest temperature at which the hydrophobic phase is sufficiently fluid to drip, as determined by test method ASTM D 566 or D 265.

The hydrophobic shell matrix is selected from the group comprising fats, oils, waxes, resins, emulsifiers or mixtures thereof, which are preferably food-grade. Preferably the hydrophobic shell matrix is selected from the group comprising animal oils and fats, fully hydrogenated vegetable or animal oils, partially hydrogenated vegetable or animal oils, unsaturated, hydrogenated or fully hydrogenated fatty acids, unsaturated, partially hydrogenated or fully hydrogenated fatty acid monoglycerides and diglycerides, unsaturated, partially hydrogenated or fully hydrogenated esterified fatty acids of monoglycerides or diglycerides, unsaturated, partially hydrogenated or fully hydrogenated free fatty acids, other emulsifiers, animal waxes, vegetable waxes, mineral waxes,

synthetic waxes, natural and synthetic resins and mixtures thereof.

Animal oils and fats are such as, but not restricted to, beef tallow, mutton tallow, lamb tallow, lard or pork fat, sperm oil. Hydrogenated or partially hydrogenated vegetable oils are such as, but not restricted to, canola oil, cottonseed oil, peanut oil, corn oil, olive oil, soybean oil, sunflower oil, safflower oil, coconut oil, palm oil, linseed oil, tung oil and castor oil. Free fatty acids are such as, but not restricted to, stearic acid, palmitic acid and oleic acid. Other emulsifiers are such as, but not restricted to, polyglycerol esters, sorbitan esters of fatty acids. Animal waxes are such as, but not restricted to, beeswax, lanolin, shell wax or Chinese insect wax. Vegetable waxes are such as, but not restricted to, carnauba, candelilla, bayberry or sugarcane waxes. Mineral waxes are such as, but not restricted to, paraffin, microcrysalline petroleum, ozocerite, ceresin or montan. Synthetic waxes are such as, but not restricted to, low molecular weight polyolefin, polyol ether-esters and Fisher-Tropsch process synthetic waxes. Natural resins are such as rosin, balsam, shellac and zein.

The encapsulated aqueous bead(s) in the microcapsules of the present invention contain encapsulating material, such as a hydrocolloid which is any food-grade hydrocolloid or any other suitable encapsulating material and which is susceptible to encapsulation by gelling, cross-linking, coacervation, sintering or by any other suitable means.

The encapsulating material is selected from the group comprising hydrocolloids, sodium alginate, gum arabic, gellan gum, starch, modified starch, guar gum, agar gum, pectin, amidified pectin, carrageenan, xanthan, gelatine, chitosan, mesquite gum, hyaluronic acid, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, psyllium, tamarind, xanthan, locust bean gum, whey protein, soy protein, sodium caseinate, any food-grade protein, shellac, zein, any synthetic or natural water-soluble polymers, any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase and susceptible to sintering and mixtures thereof.

The aqueous beads in the microcapsules of the present invention are encapsulated. In this application, encapsulation means gelling, cross-

linking, coacervation, sintering or encapsulation by any other suitable means of encapsulating. Preferably, the aqueous beads in the microcapsules of the present invention contain a hydrocolloid and the beads are preferably either gelled or cross-linked.

According to a preferred embodiment of the present invention, a microcapsule comprises a solidified hydrophobic shell matrix, a gelled or cross-linked aqueous hydrocolloid bead or beads encapsulated in the solidified hydrophobic shell matrix, and an active ingredient or active ingredients dissolved or incorporated in the gelled or cross-linked aqueous hydrocolloid bead or beads.

The gelled hydrocolloids have a gelling temperature above room temperature. Examples of gelled hydrocolloids include carrageenan, gelatine, guar gum, agar gum, starch, modified starch and mixture of xanthan and locust bean gum, mixture of carrageenan and locust bean gum and mixture of any gelling hydrocolloids and other non-gelling hydrocolloids.

The cross-linking of the hydrocolloids is carried out by using cross-linking agents or by a variety of mechanisms. If the hydrocolloid is a protein or polysaccharide bearing amino groups, it can be cross-linked by using dialdehydes, such as glutaraldehyde. If the hydrocolloid is a polysaccharide, such as sodium alginate, gellan gum or pectin, it can be cross-linked with multivalent ions, such as calcium or magnesium. The cross-linking can also be carried out by other mechanisms, such as heating, pH adjustment, applying pressure or by enzymatic cross-linking. Proteins, for example, can be cross-linked by subjecting a protein to a high pressure, preferably from 5 to 200 bar, and/or by subjecting a protein to a temperature which is above the denaturation temperature of the protein. The enzymatic cross-linking of proteins can be carried out for example with transglutamidase. Based on the hydrocolloid used, a person skilled in the art is able to decide which method of gelling or cross-linking is used.

The aqueous beads in the microcapsules of the present invention can be encapsulated by coacervation. The coacervation of the encapsulating material, such as hydrocolloid, is carried out by using any suitable coacervation process. The coacervation can be performed for example by adding salt(s), sugar(s), or other additives, which cause the phase separation of the encapsulation material, such as the hydrocolloid(s). The coacervation can also be performed by subjecting the emulsion to heating, cooling, pH change by

adding acid or base, which cause the phase separation of the encapsulating material(s), such as the hydrocolloid(s). The deposition of the coacervated phase around the aqueous phase and at the interface between the hydrophobic matrix and the aqueous phase is spontaneous and driven by surface tension forces. The coacervate layer can afterwards be subjected to cross-linking or hardening by any suitable means, which are known to persons skilled in coacervation.

The encapsulating materials suitable for coacervation are selected form the group comprising shellac, zein, any synthetic or natural hydrophobic polymers, fats, emulsifiers, waxes, any mixture of oppositely charged hydrocolloids, such as gelatine/arabic gum, gelatine/CMC, any proteins/ionic hydrocolloids, any combination of hydrocolloids and a solubility-reducing agent such as salts, sugars, acids or bases, or sucrose acetate isobutyrate (SAIB), dammar gum and glyceryl esters of wood rosin or mixtures thereof.

Sintering means in this application that the micro particles are fused together to form a porous or non-porous film. The sintering of the encapsulating material is carried out by providing a suitable amount of solid, non-soluble micro particles, which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase. The micro particles are for example such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase. The micro particles are then allowed to deposit spontaneously around the aqueous phase by subjecting the micro particles to temperatures above their sintering temperature or the glass transition temperature, thereby forming a continuous film of the micro particles.

The active ingredient or mixture of active ingredients dissolved or incorporated in the gelled, cross-linked, coacervated or sintered aqueous bead can be any ingredient, preferably a hydrophilic food or pharmaceutical ingredient, and it is selected based on the desired use of the microcapsules. The active ingredient can be for example an inorganic or organic salt or acid, such as calcium propionate, propionic acid, sorbic acid, calcium sorbate, ascorbic acid, sodium chloride, fumaric acid, potassium sorbate, citric acid or sodium bicarbonate. The active ingredient can also be a flavouring agent, such as a pizza flavour or a coffee flavour, or the active ingredient can be an antimicrobial or a preservative agent, such as nisin/natamycin, nutrient or vitamin, such as vita-

min C. A mixture of any of the above mentioned ingredients can also be used in the microcapsules.

Preferably, the active ingredient is selected from the group comprising flavours, flavour enhancers, nutrients, vitamins, preservatives, leavening agents, micro organisms, acidulants, antioxidants, colours, enzymes, gases, thickeners and any other food or pharmaceutical ingredients. Suitable pharmaceutically active ingredients include antibiotics, antimicrobials, anti-inflammatory agents, analgesics, sedatives, hypnotics, anxiolytic agents, antihistamines, antiarrhythmics, antihypertensive agents, antiparkinson agents, hormones.

The microcapsules of the present invention comprise approximately 1 to 100 aqueous beads encapsulated in the hydrophobic shell matrix, preferably 5 to 50 aqueous beads. The size of a microcapsule is approximately between 40 to 800 microns, preferably 100 to 150 microns. The size of one aqueous bead is approximately between 0.1 to 20 microns, preferably 1 to 5 microns. The number as well as the size of aqueous beads encapsulated in the solidified hydrophobic shell matrix in the microcapsule may vary, depending on the intended use of the microcapsules. The size of the microcapsules of the present invention may also vary depending on the intended use.

The present invention also relates to a novel method for preparing the microcapsules of the present invention which method comprises the steps of

a) providing an aqueous phase comprising an active ingredient or active ingredients dissolved or incorporated in the aqueous phase,

b) providing a hydrophobic phase in melted form,

c) incorporating or dissolving an encapsulating material or mixture of encapsulating materials in the aqueous phase or in the hydrophobic phase,

d) combining the aqueous phase with the hydrophobic phase and homogenizing or mixing the combined phases to form a water-in-oil emulsion,

e) encapsulating the aqueous phase in the emulsion, thus converting the liquid aqueous phase into encapsulated aqueous beads, whereby a dispersion comprising aqueous beads is formed and the active ingredient or active ingredients are encapsulated in the aqueous beads, and

f) processing the dispersion obtained in step e) to form microcapsules where the encapsulated aqueous beads are further encapsulated in the solidified hydrophobic shell matrix.

The aqueous phase means in this application water or a mixture of water and any other water-miscible solvents, such as ethanol, ethylene glycol or glycerol. The aqueous phase may also contain additives, such as carbohydrates, such as monosaccharides or oligosaccharides to modify the properties of the hydrocolloid gel, inorganic salts to modify the properties of protein gels, preservatives to avoid deterioration of the microcapsules by bacteria or fungus or emulsifiers as processing aids, sorbitan tristearate or other emulsifiers as crystal form modifier, hydrophobic natural or synthetic polymers to modify mechanical properties of the matrix, plastizisers, preservatives to avoid deterioration of the microcapsules.

The combining of the aqueous phase with the hydrophobic phase is preferably performed by mixing.

The homogenization in step d) is preferably performed by high-shear mixing or by in-line mixing.

The encapsulating material is a hydrocolloid, a mixture of hydrocolloids or any other encapsulating material or mixture thereof.

The encapsulating material is selected from the group comprising hydrocolloids, sodium alginate, gum arabic, gellan gum, starch, modified starch, guar gum, agar gum, pectin, amidified pectin, carrageenan, xanthan, gelatine, chitosan, mesquite gum, hyaluronic acid, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, psyllium, tamarind, xanthan, locust bean gum, whey protein, soy protein, sodium caseinate, any food-grade protein, shellac, zein, any synthetic or natural water-soluble polymers, any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase and susceptible to sintering and mixtures thereof.

The encapsulating in step e) is performed by gelling, cross-linking, coacervation, sintering or by any other suitable encapsulating process which results in the encapsulation of the aqueous phase comprising the active ingredient or active ingredient.

The encapsulating by gelling in step e) is performed by cooling the emulsion. The encapsulating materials suitable as gelling encapsulating materials are selected from the group comprising carrageenan, gelatine, starch,

modified starch, agar gum, guar gum and mixture of xanthan and locust bean gum or mixture of any gelling hydrocolloids.

The encapsulating by cross-linking in step e) is performed by using cross-linking agents or by a variety of mechanisms, such as heating, applying pressure or by enzymatic cross-linking. The cross-linking can be performed by subjecting the emulsion to heating at a temperature between 60 and 120°C. The cross-linking can also be performed by subjecting the emulsion to a pH value, which causes the denaturation of the hydrocolloids. The pH value is between 2 and 12. The cross-linking can also be performed by subjecting the emulsion to pressure between 2 to 200 bar.

The cross-linking agent is selected from the group comprising dialdehydes, such as glutaraldehyde, divalent ions, such as calcium or magnesium or enzymes or other cross-linking compounds, such as iridoids.

The encapsulation by gelling or cross-linking results in microcapsules, where the active ingredient is encapsulated in jelly-like beads formed from the hydrocolloid network and these are then further encapsulated in the hydrophobic shell matrix.

The encapsulating by coacervation in step e) is performed by reducing the solubility of the encapsulating material, such as the hydrocolloid, so that a coacervate phase is formed, and which coacervate phase further deposits itself around the aqueous phase. The aqueous phase in the emulsion is encapsulated forming a dispersion containing encapsulated solid aqueous beads.

The coacervation can be performed either by using a hydrophilic encapsulating material or by using a hydrophobic encapsulating material. If hydrophilic encapsulating material is used, the hydrophilic encapsulating material is first dissolved in the aqueous phase and a solubility-reducing process, such as a change in the temperature or pH or use of additives, is applied to bring the hydrophilic encapsulating material out of the aqueous phase, which is followed by the deposition of said encapsulating material at the interface between the hydrophobic phase in the melted form and the aqueous phase. After that the encapsulating material is optionally hardened by changing the temperature or pH or by adding additives. When hydrophobic encapsulating material is used, the hydrophobic encapsulating material is first dissolved in the hydrophobic phase in melted form and a solubility-reducing process, such as change in the temperature or adding additives, is applied to bring the hydrophobic encapsulating material out of the hydrophobic phase. This is followed

by deposition of said encapsulating material at the interface between the hydrophobic phase and the aqueous phase.

The encapsulating material suitable as coacervation encapsulating material is selected from the group comprising shellac, zein, any synthetic or natural polymers, cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), ethyl cellulose, methyl cellulose, carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, any mixture of oppositely charged hydrocolloids such as gelatine/arabic gum, gelatine/CMC, any proteins/ionic hydrocolloids, any combination of hydrocolloids and a solubility-reducing agent such as salts, sugars, acid or base, or sucrose acetate isobutyrate (SAIB), dammar gum, glyceryl esters of wood rosin, or mixtures thereof. In the case where fats, waxes or emulsifiers are used, they must differ from the hydrophobic matrix

The encapsulating by sintering in step e) is performed by providing a suitable amount of solid, non-soluble micro particles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase, and which micro particles are susceptible to sintering in the emulsion. After that the micro particles are allowed to deposit spontaneously around the aqueous phase at the interface between the hydrophobic phase and the aqueous phase and subjecting the micro particles to a temperature above their sintering temperature or their glass transition temperature. The micro particles are fused together to form a continuous film. A dispersion of aqueous beads encapsulated by a thin film of sintered micro particles in the hydrophobic shell matrix is thus formed.

The encapsulating materials suitable as sintering encapsulating materials are selected form the group comprising any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles which have a particle size substantially smaller than the size of the aqueous droplets in the aqueous phase in the hydrophobic matrix.

The encapsulation by coacervation or sintering results in microcapsules, where a thin coating of the encapsulating material is deposited around the aqueous beads comprising active ingredient(s) and the bead or the beads is/are further encapsulated in the hydrophobic shell matrix.

The forming of the dispersion of the combined solution in step e) is

performed by any suitable process or means which reduce the solubility of the dissolved encapsulating material resulting in the deposition of the encapsulating material around the aqueous phase. Preferably step e) is performed by a temperature change, either by decreasing or increasing the temperature, or by addition of additives.

The processing in step f) is carried out by any suitable method, which results in the solidification of the hydrophobic phase forming a hydrophobic shell matrix and the formation of the microcapsule. Preferably the processing is done by spray cooling or by fluidized bed cooling.

The hydrophobic phase is selected based on desired properties of the microcapsules, for example based on the intended use of the microcapsules, storage temperature, etc. The hydrophobic phase should preferably have a melting point above 45°C so that it can be easily stored at room temperature.

In this application, melted form means that the hydrophobic phase is at the lowest temperature at which the hydrophobic phase is sufficiently fluid to drip, as determined by test method ASTM D 566 or D 265.

The hydrophobic phase is selected from the group comprising fats, oils, waxes, resins, emulsifiers or mixtures thereof, which are preferably food-grade. Preferably the hydrophobic phase is selected from the group comprising animal oils and fats, fully hydrogenated vegetable or animal oils, partially hydrogenated vegetable or animal oils, unsaturated, partially hydrogenated or fully hydrogenated fatty acid monoglycerides and diglycerides, unsaturated, partially hydrogenated or fully hydrogenated esterified fatty acids of monoglycerides or diglycerides, unsaturated, partially hydrogenated or fully hydrogenated free fatty acids, other emulsifiers, animal waxes, vegetable waxes, mineral waxes, synthetic waxes, natural and synthetic resins, and mixtures thereof.

Animal oils and fats are such as beef tallow, mutton tallow, lamb tallow, lard or pork fat, sperm oil. Vegetable oils are such as canola oil, cottonseed oil, peanut oil, corn oil, olive oil, soybean oil, sunflower oil, safflower oil, coconut oil, palm oil, linseed oil, tung oil and castor oil. Free fatty acids are such as stearic acid, palmitic acid and oleic acid, other emulsifiers such as fatty acid esters of sorbitan and polygycerol esters, animal waxes, such as beeswax, lanolin, shell wax or Chinese insect wax. Vegetable waxes are such as carnauba, candelilla, bayberry or sugarcane. Mineral waxes are such as

paraffin, microcrysalline petroleum, ozocerite, ceresin or montan. Synthetic waxes are such as low molecular weight polyolefin, polyol ether-esters and Fisher-Tropsch process synthetic waxes. Natural resins are such as rosin, balsam and shellac and zein.

The active ingredient or mixture of active ingredients can be any hydrophilic ingredient, preferably a food-grade or pharmaceutical ingredient, and it is selected based on the desired use of the microcapsules. The active ingredient can be for example a salt or an acid, such as calcium propionate, propionic acid, sorbic acid, calcium sorbate, ascorbic acid, sodium chloride, fumaric acid, potassium sorbate, citric acid or sodium bicarbonate. The active ingredient can also be a flavouring agent, such as pizza flavour or coffee flavour, or the active ingredient can be an antimicrobial or a preservative agent, such as a bacteriocin (e.g. nisin or pediocin), natamycin, nutrient or vitamin, such as vitamin C.

Preferably, the active ingredient is selected from the group comprising flavours, flavour enhancers, nutrients, vitamins, preservatives, leavening agents, micro organisms, acidulants, antioxidants, colours, enzymes, gases, thickeners and any other food or pharmaceutical ingredients. Suitable pharmaceutically active ingredients include antibiotics, antimicrobials, anti-inflammatory agents, analgesics, sedatives, hypnotics, anxiolytic agents, antihistamines, antiarrhythmics, antihypertensive agents, antiparkinson agents and hormones.

Preferably the present invention relates to a method which comprises the steps of

a) providing an aqueous phase comprising a hydrocolloid or a mixture of hydrocolloids and an active ingredient or active ingredients,

b) providing a hydrophobic phase in melted form,

c) combining the aqueous phase of step a) with the hydrophobic matrix of step b) and homogenizing the combined solution to form an emulsion,

d) gelling or cross-linking the hydrocolloids in the emulsion, whereby a dispersion comprising gelled or cross-linked hydrocolloid beads is formed and the active ingredient or active ingredients are dissolved or incorporated in the gelled or cross-linked hydrocolloid beads, and

e) cooling the dispersion obtained in step d) by spray cooling or fluidized bed cooling to form microcapsules where the gelled or cross-linked hydrocolloid beads are encapsulated in the solidified hydrophobic shell matrix.

The combining of the aqueous phase of step a) with the hydrophobic phase of step b) is preferably performed by mixing.

The homogenization in step c) is preferably performed by high-shear mixing or by in-line mixing.

The hydrocolloid to be used in the present invention is any food-grade hydrocolloid and it is preferably water-soluble and susceptible to gelling and/or cross-linking.

The hydrocolloid is selected from the group comprising sodium alginate, arabic gum, gellan gum, starch, modified starch, guar gum, pectin, amidified pectin, carrageenan, gelatine, chitosan, mesquite gum, agar gum, hyaluronic acid, whey protein, soy protein, sodium caseinate, xanthan/locust bean gum mixture, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, psyllium, tamarind, xanthan, locust bean gum, whey protein, soy protein, sodium caseinate, any food-grade protein, shellac, zein, any synthetic or natural water-soluble polymers, and mixtures thereof.

The hydrocolloid comprised in the emulsion is preferably either gelled or cross-linked. The hydrocolloids to be gelled have a gelling temperature above the storage temperature. Examples of gelling hydrocolloids include carrageenan, gelatine, starch, modified starch, agar gum, guar gum and mixture of xanthan and locust bean gum or mixture of any gelling hydrocolloids and any other non-gelling hydrocolloids. The gelling of the hydrocolloids in the emulsion is performed by the cooling of the emulsion, either before or during the cooling step. If the gelling of the hydrocolloid is carried out during the cooling, the emulsion is cooled after being formed. If the gelling of the hydrocolloid is carried out before the spray cooling, a dispersion is formed which comprises gelled hydrocolloid beads, and this dispersion is then cooled to form microcapsules.

The cross-linking of the hydrocolloids is carried out by using cross-linking agents or by a variety of mechanisms. If the hydrocolloid is a protein or a polysaccharide containing amino groups, such as chitosan, acic, arabic gum or mesquite gum, it can be cross-linked by using dialdehydes, such as glutaraldehyde. If the hydrocolloid is a polysaccharide, such as sodium alginate, gellan gum or pectin, it can be cross-linked with multivalent ions, such as calcium and magnesium. The cross-linking can also be carried out by other

mechanisms, such as by heating, by applying pressure or by enzymatic cross-linking. Proteins, for example, can be cross-linked by subjecting to high pressure, preferably from 2 to 200 bar, and/or by subjecting a protein to a temperature which is above the denaturation temperature of the protein. The temperature during the heating depends on the hydrocolloid to be cross-linked. The enzymatic cross-linking of proteins can be carried out for example with transglutamidase. A person skilled in the art is able to decide which method of gelling or cross-linking is used based on the hydrocolloid used.

The cross-linking agent is selected from the group comprising dialdehydes, such as glutaraldehyde, divalent ions, such as calcium or magnesium or other cross-linking compounds, such as irridoids.

The cooling of the dispersion is preferably performed by spray cooling in a spray cooling tower or by fluidized bed cooling in a fluidized bed apparatus. During the spray cooling the hydrophobic matrix, which is in a melted form in the dispersion, is cooled so that it solidifies into particle form, encapsulating the hydrocolloid bead. Room temperature gas or cooled gas can be used in the cooling tower. Preferably the gas or the cooling gas is air. The temperature of the cooling gas is between -270 and 50°C, preferably between -50 and 40°C and more preferably between -20 and 20°C.

The hydrophobic phase is selected as described above.

The active ingredient is selected as described above.

The properties of the microcapsules can be altered by altering the process parameters of the above-described methods. For example, pastizisers can be added into the hydrophobic matrix phase to improve flexibility and to modify mechanical properties of the outer shell, lipase enzymes can be added in to the aqueous phase to modify the release rate.

One microcapsule prepared according to the method of the present invention comprises approximately 1 to 100 aqueous beads embedded in the hydrophobic shell matrix, preferably 5 to 50 aqueous beads. The size of the microcapsule is approximately 40 to 800 microns, preferably 100 to 150 microns. The size of one aqueous bead is approximately 0.1 to 20 microns, preferably 1 to 5 microns.

The present invention also relates to the use of the microcapsules of the present invention. The microcapsules described above can be used in a wide variety of applications in food industry and in pharmaceutical applications.

The microcapsules of the present invention can be used in a great

variety of applications, depending for example on the properties of the microcapsules, the active ingredient or a mixture thereof, the hydrocolloid, the hydrophobic matrix or the size of the microcapsules. A controlled release of the active ingredients from the microcapsules is achieved by the present invention. The release of the active ingredients from the microcapsules can be controlled by initiating the release in various ways, for example by heat treatment, by heating in a microwave oven, or by any other suitable process. The release of the active ingredients from the microcapsules of the present invention can also happen very slowly. The release of the ingredient also takes place upon freezing of the microcapsules. Freezing causes the water phase to expand, which causes the external hydrophobic matrix to crack. Upon thawing, the active ingredient is quickly released from the microcapsule.

In bakery, for example, delayed release of antimolding agent can be achieved with the microcapsules of the present invention. This is very important in order to avoid inhibition of the required activity of the baker's yeast. If nisin or natamycin is used as the active ingredients, increased heat stability is achieved for example in pasteurised or heat-processed foods. Delayed release of sodium chloride is also very important for example in cheeses to avoid harmful interaction with starting cultures. Thermal stability of vitamin C in bakery/confectionary can be achieved with the microcapsules of the present invention.

The present invention relates to the use of microcapsules as flavours, bacteriocin agents, preservative agents and agents providing slow, controlled and/or sustained release of the active ingredient(s). The microcapsules of the present invention are used in a wide variety of pharmaceutical applications where slow, controlled and/or sustained release of the pharmaceutically active ingredient is required. Such uses include for example depot-tablets and trans-dermal application systems.

Controlled release of flavours in food products, such as baked goods, pizza, instant coffee, tea bags, is achieved with the microcapsules of the present invention containing flavours as the active ingredient. The encapsulated flavours are retained in the product until heat and/or stress treatment is applied to release the flavours. Heat can be provided for example by a microwave-oven, conventional oven or hot water. Stress can be provided for example by processing conditions or mastication.

Slow release of bacteriocin for example in processed meat products or in beverages, such as orange juice, is achieved with the microcapsules of the present invention. If a preservative agent is used as an active ingredient in the microcapsules of the present invention, the preservative agent is slowly released in the product as it is naturally degraded. This effectively prevents growth of fungi or other undesirable micro organisms for a longer period of time than a non-encapsulated preservative, thus ensuring a longer shelf life for the food product. The coating can also provide thermal stability to bacteriocin and preservative agents so as to survive heat treatment and harsh processing conditions, but to remain active during storage of the processed product.

The microcapsules of the present invention provide delayed release of salt in cheese production, which allows a 1-step process instead of a 2-step process. The delayed release of salt allows the starter culture to work properly at the beginning without being subjected to the detrimental effect of salt. When fermentation is over, the salt is released. In a typical process, salt is added after fermentation by time-consuming dipping of the cheese in brine.

Delayed release of an anti-microbial agent in bakery applications is achieved by the microcapsules of the present invention. The preservatives are widely used to extend the shelf life of breads and other bakery products, but at the expense of detrimentally affecting the effectiveness of the yeast. The delayed release allows a more efficient use of the yeast, while also providing the preservative properties after the active ingredient is released during baking. As an added benefit, propionic acid, which is much more potent than its calcium salt but much more difficult to handle due to its high acidity and liquid form, can be transformed into a stable powder which is easy to handle.

The pharmaceutically active ingredients encapsulated according to the present invention provide slow, controlled and/or sustained release of the active ingredient over time, for example in depot-tablets, in a much cheaper way compared to how it is performed today (by fluidized bed coating). The encapsulation according to the present invention also provides stability of the pharmaceutically active ingredients in the gastric tract (low pH), which enables them to be released later on in the intestinal tract where most of the pharmaceutically active ingredients are actually absorbed. Examples of suitable pharmaceutically active ingredients include antibiotics, antimicrobials, anti-inflammatory agents, analgesics, sedatives, hypnotics, anxiolytic agents, antihistamines, antiarrhythmics, antihypertensive agents, antiparkinson agents and

hormones.

Examples

Example 1 – Encapsulation of pizza flavour.

First, a solution of 1.5 g κ-carrageenan in 110 ml of water is prepared at 85°C. To this is added 110 ml of a pre-heated (80°C) water-soluble liquid pizza flavour. The resulting mixture is thoroughly mixed. Secondly, a mixture of 200 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 11 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mixture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 0,45 g of polysorbate 80 in 15 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A pizza-smelling free flowing powder is obtained.

A 6" frozen model pizza is sprinkled 1.5 g of the flavoring powder and baked in the microwave for 2 minutes at medium-high intensity. The flavored pizza samples have a distinctly stronger pizza aroma when exiting the microwave compared to control pizza samples.

Example 2 – Encapsulation of coffee flavor.

First, a solution of 1.5 g κ-carrageenan in 110 ml of water is prepared at 85°C. To this is added 110 ml of a pre-heated (80°C) water-soluble coffee flavor. The resulting mixture is thoroughly mixed. Secondly, a mixture of 200 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 11 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8 kRPM) as the aqueous mixture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 0.45 g of polysorbate 80 in 15 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air tempera-

ture 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A coffee-smelling free flowing powder is obtained.

The flavoring powder is added to hot water (90°C) and a strong coffee aroma evolves within one minute.

Example 3. – Encapsulation of nisin

First, a solution of 15 g κ-carrageenan in 1000 ml of phtalate buffer at pH 3.5 is prepared at 85°C. To this is added 300 g of commercial nisin extract (Nisaplin®, Danisco). The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mixture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained. The incorporation of encapsulated nisin in a suspension media for subsequent spraying onto food products such as sausages, sausage casings, meat products or any other food products requiring bactericides results in a much more stable nisin formulation compared to when unencapsulated or conventionally spray cooled nisin is used in the suspension media, thus dramatically improving survival rate of nisin until the pasteurisation of the food product. For example, spray cooled nisin is released in the suspension media, thus subjecting it to rapid degradation, at a rate of 57% after 3 days in the suspension media. The encapsulated nisin, as presented in this example, is released at a rate of only 7% after tree days.

Example 4. – Encapsulation of nisin

First, a solution of 15 g sodium alginate in 1000 ml of phtalate buffer at pH 3.5 is prepared at 85°C. To this is added 300 g of commercial nisin extract (Nisaplin®, Danisco). The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization

(Silverson mixer, 8 kRPM) as the aqueous mixture is slowly incorporated. Following the incorporation of the aqueous mixture, a solution of 7 g of calcium chloride in 70 ml of water is added dropwise. The homogenization is maintained for another 5 minutes and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained. As mentioned previously, encapsulated nisin as presented in this example is much more stable in aqueous environment than a conventionally spray-cooled sample. For example, spray cooled nisin is released in the suspension media, thus subjecting it to rapid degradation, at a rate of 57% after 3 days in the suspension media. The encapsulated nisin, as presented in this example, is released at a rate of only 0,1% after tree days.

Example 5. – Encapsulation of sodium chloride

First, a solution of 15 g κ-carrageenan in 1000 ml of water is prepared at 85°C. To this is added 585 g of sodium chloride. The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mixture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained.

Example 6. – Encapsulation of sorbic acid

First, a solution of 15 g κ-carrageenan in 1000 ml of water is prepared at 85°C. To this is added 300 g of sorbic acid. The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mix-

ture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained.

Example 7. Encapsulation of calcium propionate

First, a solution of 15 g κ-carrageenan in 1000 ml of water is prepared at 85°C. To this is added 300 g of calcium propionate. The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mixture is slowly incorporated. The homogenization is maintained for 5 minutes after the whole aqueous mixture is added and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters: inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained. The release rate of the calcium propionate is determined using the basket method. The curve is shown in Figure 1.

Example 8. Encapsulation of propionic acid

First, a solution of 40 g of amidified low ester pectin (Danisco Pectin 2580) in 750 ml of water is prepared at 85°C. To this is added 250 g of propionic acid. The resulting mixture is thoroughly mixed. At the same time, a mixture of 1333 g of a vegetable triglyceride (GRINDSTED ® PS 101, m.p. 58°C) and 73 g of acetylated emulsifier (Acetem 50 00) is melted at 85°C in a water bath. The melted fat mixture is kept under homogenization (Silverson mixer, 8000 rpm) as the aqueous mixture is slowly incorporated. Following the incorporation of the aqueous mixture, a solution of 5 g of calcium chloride in 30 ml of water is added dropwise. The homogenization is maintained for another 5 minutes and then a solution of 3 g of polysorbate 80 in 40 ml of water is added under constant mixing. The resulting low-viscosity water-in-oil emulsion is then immediately spray cooled in a Niro spray tower using the following parameters:

inlet air temperature 10°C, outlet air temperature 28°C, rotating atomization wheel speed 10 000 rpm. A free flowing powder is obtained.

It will be obvious to a person skilled in the art that as technology advances, the inventive concept can be implemented in various ways. The invention and its embodiments are not limited to the examples described above but may vary within the scope of the claims.

Claims

1. A microcapsule comprising

a solidified hydrophobic shell matrix,

an encapsulated aqueous bead or beads which is/are further encapsulated in the solidified hydrophobic shell matrix, and

an active ingredient or active ingredients dissolved or incorporated in the encapsulated aqueous bead or beads.

2. A microcapsule according to claim 1, characterized in that the encapsulated aqueous bead is an aqueous hydrocolloid bead.

3. A microcapsule according to claim 1 or 2, characterized in that the encapsulated hydrocolloid bead is a gelled or cross-linked hydrocolloid bead.

4. A microcapsule according to claim 1 or 2, characterized in that the encapsulated aqueous bead is encapsulated by coacervation using a suitable encapsulating material.

5. The microcapsule according to claim 4, characterized in that the encapsulating material used in coacervation is selected from the group comprising shellac, zein, any synthetic or natural hydrophobic polymers, fats, emulsifiers, waxes, any mixture of oppositely charged hydrocolloids, such as gelatine/arabic gum, gelatine/CMC, any proteins/ionic hydrocolloids, any combination of hydrocolloids and a solubility-reducing agent such as salts, sugars, acids or bases, or sucrose acetate isobutyrate (SAIB), dammar gum and glyceryl esters of wood rosin or mixtures thereof.

6. A microcapsule according to claim 1 or 2 characterized in that the encapsulated aqueous bead is encapsulated by sintering using a suitable encapsulating material.

7. The microcapsule according to claim 6, characterized in that the encapsulating material used in sintering is selected from the group comprising any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles.

8. The microcapsule according to any one of the preceding claims 1 to 3, characterized in that the encapsulated aqueous bead comprises any food-grade hydrocolloid which has a gelling temperature above storage temperature.

9. The microcapsule according to any one of the preceding claims 1

to 3, characterized in that the encapsulated aqueous bead comprises any food-grade hydrocolloid which can be cross-linked.

10. The microcapsule according to any one of claims 8 or 9, characterized in that the hydrocolloid is selected from the group comprising sodium alginate, arabic gum, gellan gum, starch, modified starch, guar gum, pectin, amidified pectin, carrageenan, gelatine, chitosan, mesquite gum, agar gum, hyaluronic acid, whey protein, soy protein, sodium caseinate, xanthan/locust bean gum mixture, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, psyllium, tamarind, xanthan, locust bean gum, whey protein, soy protein, sodium caseinate, shellac, zein, any synthetic or natural water-soluble polymers, any food-grade protein, and mixtures thereof.

11. The microcapsule according to any one of the preceding claims, characterized in that the hydrophobic shell matrix is selected from the group comprising animal oils and fats, fully hydrogenated vegetable or animal oils, partially hydrogenated vegetable or animal oils, unsaturated, hydrogenated or fully hydrogenated fatty acids, unsaturated, partially hydrogenated or fully hydrogenated fatty acid monoglycerides and diglycerides, unsaturated, partially hydrogenated or fully hydrogenated esterified fatty acids of monoglycerides or diglycerides, unsaturated, partially hydrogenated or fully hydrogenated free fatty acids, other emulsifiers, animal waxes, vegetable waxes, mineral waxes, synthetic waxes, natural and synthetic resins, and mixtures thereof.

12. The microcapsule according to any one of the preceding claims, characterized in that the active ingredient is selected from the group comprising flavours, flavour enhancers, nutrients, vitamins, preservatives, leavening agents, micro organisms, acidulants, antioxidants, colours, enzymes, gases, thickeners and any other food or pharmaceutical ingredients, such as antibiotics, antimicrobials, anti-inflammatory agents, analgesics, sedatives, hypnotics, anxiolytic agents, antihistamines, antiarrhythmics, antihypertensive agents, antiparkinson agents and hormones.

13. The microcapsule according to any one of the preceding claims, characterized in that one microcapsule comprises approximately 1 to 100 aqueous beads embedded in the hydrophobic shell matrix, preferably 5 to 50 aqueous beads.

14. A method for preparing microcapsules, comprising the steps of

a) providing an aqueous phase and an active ingredient or active ingredients dissolved or incorporated in the aqueous phase,

b) providing a hydrophobic phase in melted form,

c) incorporating or dissolving an encapsulating material or a mixture of encapsulating materials in the aqueous phase or in the hydrophobic phase,

d) combining the aqueous phase with the hydrophobic phase and homogenizing or mixing the combined phases to form a water-in-oil emulsion,

e) encapsulating the aqueous phase in the emulsion, whereby a dispersion comprising encapsulated aqueous beads is formed and the active ingredient or active ingredients are encapsulated in the aqueous beads, and

f) processing the dispersion obtained in step e) to form microcapsules where the encapsulated aqueous beads are further encapsulated in the solidified hydrophobic shell matrix.

15. A method according to claim 14, characterized in that the aqueous phase is selected from the group comprising water or a mixture of water and any other water-miscible solvents, such as ethanol, ethylene glycol, glycerol.

16. A method according to claim 14 or 15, characterized in that the encapsulating material is selected from the group comprising hydrocolloids, sodium alginate, gum arabic, gellan gum, starch, modified starch, guar gum, agar gum, pectin, amidified pectin, carrageenan, xanthan, gelatine, chitosan, mesquite gum, hyaluronic acid, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methylcellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit®, psyllium, tamarind, xanthan, locust bean gum, whey protein, soy protein, sodium caseinate, any food-grade protein, shellac, zein, any synthetic or natural water-soluble polymers, any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles susceptible to sintering.

17. A method according to any one of preceding claims 14 to 16, characterized in that the hydrophobic phase is selected from the group comprising animal oils and fats, fully hydrogenated vegetable or animal oils, partially hydrogenated vegetable or animal oils, unsaturated, hydrogenated or fully hydrogenated fatty acids, unsaturated, partially hydrogenated or fully hydrogenated fatty acid monoglycerides and diglycerides, unsaturated, partially hydrogenated or fully hydrogenated esterified fatty acids of monoglycerides or di-

glycerides, unsaturated, partially hydrogenated or fully hydrogenated free fatty acids, other emulsifiers, animal waxes, vegetable waxes, mineral waxes, synthetic waxes, natural and synthetic resins, and mixtures thereof.

18. A method according to any one of the claims 14 to 17, characterized in that the combining of the aqueous phase with the hydrophobic phase is performed by mixing.

19. A method according to any one of claims 14 to 18, characterized in that the homogenization in step d) is performed by high-shear mixing or by in-line mixing.

20. A method according to any one of preceding claims 14 to 19, characterized in that the encapsulating is performed by gelling, cross-linking, coacervation or by sintering.

21. A method according to claim 20, characterized in that encapsulating by coacervation is performed by using an encapsulating material and reducing the solubility of the encapsulating material.

22. A method according to claim 21, characterized in that the solubility of the encapsulating material is reduced by changing the temperature, by changing the pH, by adding additives or by adding hydrocolloids or any suitable coacervation-inducing agent.

23. A method according to claim 21 or 22 characterized in that the encapsulating material is selected from the group comprising shellac, zein, any synthetic or natural hydrophobic polymers, as well as fats, emulsifiers, waxes or mixture thereof.

24. A method according to claim 20, characterized in that encapsulating by sintering is performed by using solid microparticles as an encapsulating material.

25. A method according to claim 24 characterized in that the microparticles are fused into a continuous film around the aqueous phase by subjecting the microparticles to temperatures above their sintering or glass transition temperatures.

26. A method according to claim 24 or 25 characterized in that the encapsulating material is selected from the group comprising any water-insoluble microparticles, such as silicone dioxide, titanium dioxide, synthetic or natural food-grade polymer beads or any water-insoluble solid particles.

27. The method according to claim 20, characterized in that the encapsulating of the aqueous phase is performed by gelling and the gelling of the

aqueous phase in the emulsion is performed by lowering the temperature of the emulsion below the gelling temperature of the encapsulating material.

28. The method according to claim 27 characterized in that the encapsulating material is selected from the group comprising gelling hydrocolloids, such as carrageenan, gelatine, starch, modified starch, agar gum, guar gum and mixture of xanthan and locust bean gum or mixture of any gelling hydrocolloids.

29. The method according to claim 20, characterized in that the encapsulating of the aqueous phase is performed by cross-linking by using an encapsulating material selected from the group comprising any food-grade proteins such as soy protein, whey proteins, caseinate gelatine, or starch, modified starch, chitosan, cellulose derivatives such as cellulose acetate phtalate, hydroxy propyl methyl cellulose (HPMC), methyl cellulose, ethyl cellulose and carboxy methyl cellulose (CMC), methyl acrylic copolymers, such as Eudragit, any synthetic or natural water-soluble polymers, susceptible to cross-linking by heat, pH or chemical treatment and mixture thereof.

30. The method according to claim 29 characterized in that the cross-linking is performed by heating, applying pressure or by enzymatic cross-linking.

31. The method according to any one of preceding claims 14 to 30, characterized in that the processing in step f) is performed by spray cooling.

32. The method according to any one of preceding claims 14 to 30, characterized in that the processing in step f) is performed by fluidized bed cooling.

33. The method according to any one of preceding claims 14 to 32, characterized in that the active ingredient is selected from the group comprising flavours, flavour enhancers, nutrients, vitamins, preservatives, leavening agents, micro organisms, acidulants, antioxidants, colours, enzymes, gases, thickeners and any other food or pharmaceutical ingredients.

34. The method according to any one of preceding claims 14 to 33, characterized in that one microcapsule comprises approximately 1 to 100 aqueous beads embedded in the hydrophobic shell matrix, preferably 5 to 50 aqueous beads.

35. Use of the microcapsules as described in any one of the preceding claims as additives in food industry.

36 Use of the microcapsules according to claim 35 as a flavour agent, a preservative agent or a bacteriocin agent.

37. Use of the microcapsules as described in any one of the preceding claims in pharmaceutical applications.

38. Use of the microcapsules according to claim 37 in depot-tablets or trans-dermal application systems.

39. A microcapsule substantially as hereinbefore described with reference to the accompanying drawings.

40. A method for producing a microcapsule substantially as hereinbefore described with reference to the accompanying drawings.

41. Use of a microcapsule substantially as hereinbefore described with reference to the accompanying drawings.

Abstract

The present invention relates to microcapsules, and more particularly to microcapsules where an aqueous bead or beads comprising the active ingredient is encapsulated in a hydrophobic shell matrix. The present invention relates also to novel methods for preparing the microcapsules according to the invention, as well as to the use of the microcapsules of the present invention. A microcapsule of the present invention comprises a solidified hydrophobic shell matrix, an encapsulated aqueous bead or beads which is/are encapsulated in the solidified hydrophobic shell matrix, and an active ingredient or active ingredients dissolved or incorporated in the encapsulated aqueous bead or beads.

Figure 1. Comparing Release Rates for Encapsulated and conventionally spray cooled Calcium Propionate

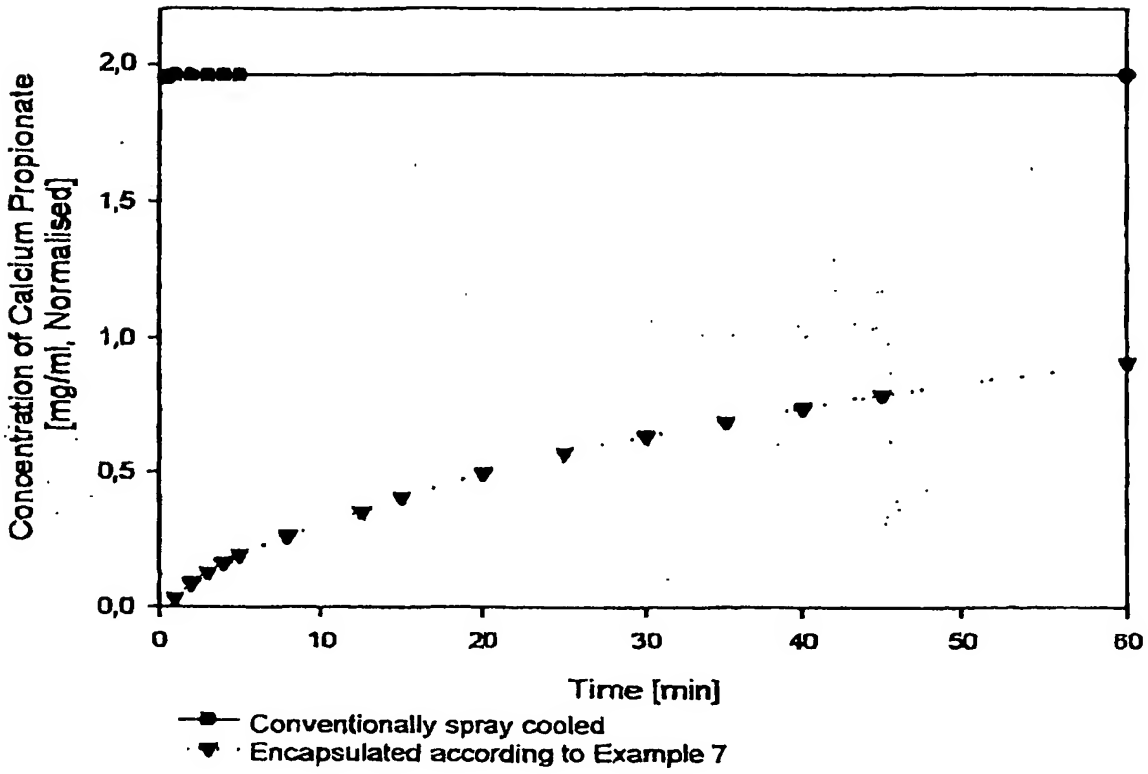

FIG. 1

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